REMARKS

In accordance with the present invention, there are provided methods for testing a compound for its ability to regulate transcription-activating effects of a peroxisome proliferator activated receptor-gamma (PPAR-γ). Invention methods comprise assaying for changes in the level of reporter protein present as a result of contacting cells containing PPAR-γ and a reporter vector with the compound of interest. Compounds identified employing invention methods are useful in the treatment of pathological conditions such as, for example, diabetes.

Responsive to the Examiner's comments regarding the declaration and drawings, a new declaration and formal drawings will be provided in due course, when the application is otherwise in condition for allowance.

By the present communication, the title of the invention has been amended. The Examiner's suggestion of acceptable language for use in the title is acknowledged with appreciation. In addition, the specification has been amended to update the status of the parent applications.

Claims 18 and 19 have been amended merely to make reference to the relevant sequence identifiers for the nucleic acid sequences recited therein, and new claims 27 and 28 have been added to define Applicants' invention with greater particularity. In addition, claim 21 has been cancelled without prejudice. No new matter has been introduced as the amended claim language is fully supported by the specification and original claims. Upon entry of this amendment, claims 16-20, 27, and 28 will be pending.

The Examiner's assertion that the present application allegedly does not contain an abstract of the disclosure is respectfully submitted to be in error. The present application is a national stage application of the corresponding PCT international application. Accordingly, consistent with PCT practice, the abstract is provided on the cover sheet of the application.

However, to reduce the issues and expedite prosecution, a copy of the abstract is enclosed herewith on a separate sheet.

The rejection of claims 16-21 under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention, is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that a "large quantity of experimentation is necessary to determine the sequence of the optimal response element and to regulate transcription activation of PPAR-γ by assaying the levels of a reporter protein, wherein the reporter vector comprises a promoter, a hormone response element, and a DNA segment encoding the reporter" (see Office Action mailed August 15, 2001, page 6 , line 21 to page 7, line 2). Contrary to the Examiner's assertion, it is respectfully submitted that the specification fully enables the entire scope and breadth of claims 16-21 in a clear, concise, and stepwise fashion. Accordingly, a "large quantity of experimentation" is most certainly not required to practice the invention as defined by claims 16-21.

It is respectfully submitted that Examples 1-4 in the specification provide substantial guidance with respect to various aspects of the claimed methods. For instance, Example 1 describes the preparation of a GAL4-receptor fusion protein. Those skilled in the art readily recognize that the process described in Example 1 is useful for generating a number of chimeric species, including GAL4-PPAR-γ, which contains residues 163-475 of PPAR-γ. Indeed, this aspect of the invention is described in detail (see specification, page 22, lines 2-34). Accordingly, those skilled in the art would not require a "large quantity of experimentation" to practice this aspect of the invention.

Example 2 describes preparation of various reporter constructs. Since those skilled in the art are quite familiar with methods for the preparation of reporter constructs, the description in Example 2 provides ample guidance regarding this aspect of the claimed invention. Thus, a

"large quantity of experimentation" is decidedly not required to practice this aspect of the invention.

Similarly, Example 3 describes in detail a screening assay for identification of receptor selective agonists. In view of the guidance provided by Example 3, those skilled in the art would readily acknowledge that a "large quantity of experimentation" is clearly not required to practice this aspect of the invention.

Finally, Example 4 fully describes the measurement of dose responses of GAL4-PPAR-γ constructs to various compounds (in this Example, the compounds are prostaglandins). The process for gathering this data as well as the interpretation of the data is lucidly presented in Example 4.

It is respectfully submitted that the combined teachings of Examples 1-4, in view of the rest of the specification, provide ample guidance to those skilled in the art such that a "large quantity of experimentation" is clearly not necessary to practice the present invention. Accordingly, reconsideration and withdrawal of the rejection of claims 16-21 under 35 U.S.C. 112, first paragraph, are respectfully requested.

The rejection of claims 16-21 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim subject matter which Applicants regard as the invention, is respectfully traversed. It is respectfully submitted that the claims are clear and unambiguous as written. With specific reference to the term "thereof" as used in claim 16, those skilled in the art readily recognize that this term, when read in context, clearly refers to the promoter, which is activated when operatively associated with an activated hormone response element.

In addition, Applicants respectfully disagree with the Examiner's assertion that claims 16-21 are allegedly indefinite since the claims do not have a step that relates back to the

preamble. It is respectfully submitted that there is no statutory requirement that a claim drawn to a method must have a step relating back to the preamble. Moreover, with respect to the level of reporter protein, it is respectfully submitted to be clear that when claim 16 is read in its entirety, one must merely determine if a test compound causes a change in the level of reporter protein to conclude that a test compound regulates transcription-activating effects of PPAR-γ (see for example, specification, page 24, line 27 to page 25, line 14).

With respect to the term "modulator" as used in claim 21, Applicants respectfully disagree with the Examiner's assertion that this term allegedly renders the claim indefinite. Those skilled in the art readily recognize there are a number of compounds which have been well-established as PPAR-γ selective modulators. Indeed, those skilled in the art could readily identify compounds which fall within the scope of claim 21. Moreover, these are merely added components in the invention assay. Accordingly, contrary to the Examiner's assertion, the use of the term "modulator" does not create ambiguity with respect to claim 21. Nonetheless, with specific reference to claim 21, the rejection has been rendered moot by the cancellation of claim 21, and it is respectfully submitted that the rejection does not apply to new claims 27 and 28.

For all of the above reasons, it is respectfully submitted that the rejection under 35 U.S.C. 112, second paragraph, is not properly applied. Accordingly, reconsideration and withdrawal of the rejection of claims 16-21 under 35 U.S.C. 112, second paragraph, are respectfully requested.

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In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. If any matters remain to be resolved, the Examiner is invited to contact the undersigned at the telephone number set forth below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Enclosures: Appendix, Abstract

APPENDIX

16. (Reiterated) A method of testing a compound for its ability to regulate transcription-activating effects of a peroxisome proliferator activated receptor-gamma (PPAR-γ), said method comprising assaying for changes in the level of reporter protein present as a result of contacting cells containing said receptor and reporter vector with said compound;

wherein said reporter vector comprises:

(a) a promoter that is operable in said cell,

(b) a hormone response element, and

(c) a DNA segment encoding a reporter protein,

wherein said reporter protein-encoding DNA segment is operatively linked to said promoter for transcription of said DNA segment, and

wherein said hormone response element is operatively linked to said promoter for activation thereof.

17. (Reiterated) A method according to Claim 16 wherein said hormone response element is a direct repeat of two or more half sites separated by a spacer of one nucleotide, wherein said spacer can be A, C, G or T, wherein each half site comprises the sequence

-RGBNNM-,

wherein

R is selected from A or G;

B is selected from G, C, or T;

each N is independently selected from A, T, C, or G; and

M is selected from A or C;

with the proviso that at least 4 nucleotides of said -RGBNNM- sequence are identical with the nucleotides at corresponding positions of the sequence -AGGTCA-; and

wherein said response element is optionally preceded by N_x, wherein x falls in the range of 0 up to 5.